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| EXAMINER | |
|---|---|
| MOHAMED, ABDEL A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1653 | |

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/857,115 | QI ET AL. | |
| | Examiner | Art Unit | |
| | Abdel A. Mohamed | 1653 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3, 6*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

## ACKNOWLEDGMENT FOR PRIORITY, PRELIMINARY AMENDMENTS, SEQUENCE LISTING, IDS, RESTRICTION REQUIREMENT, STATUS OF THE APPLICATION AND CLAIMS.

1. This application is filed under 35 U.S.C. 371 on 12/26/01 having a filing date of 2/12/99 of PCT/GB99/04045. Acknowledgement is made of Applicant's claim for priority based on United Kingdom Application No. 9826662.01 having a filing date of 12/3/98. Receipt is acknowledged of papers submitted under 35 U.S.C. § 119, which papers have been placed of record in the file. The preliminary amendments filed 12/26/01 and 1/28/02; the information disclosure statements (IDS) and Form PTO-1449 filed 12/26/01 and 9/4/03; the sequence listing filed 3/19/03 and the response to the restriction requirement filed 12/23/03 are acknowledged, entered and considered. In view of Applicant's request claims 1, 2, 7, 8, 10 and 12 have been amended. Thus, claims 1-13 are now pending in the application.

## ELECTION WITH TRAVERSE

2. Applicant's election with traverse of Group I (claims 1-5) in Paper No. 6 is acknowledged. The traversal presented in the election has been considered persuasive for the reasons set forth in the traverse. Hence, the Office action is directed to the merits of claims 1-13 and the previous requirement for restriction has been withdrawn.

## OBJECTION TO THE TITLE

3. The title is objected in using the abbreviation "GnRH-II". Us of full terminology by amending the title to recite" Controlled release formulation comprising gonadotropin-releasing hormone-II" is suggested.

## OBJECTION TO THE SPECIFICATION

4. The disclosure is objected to because of the following informalities: On page 2, last line and page 4, third paragraph in the recitation "(7)" after the sequence. Amendment of the specification by using a sequence identifier instead of (7) (e.g., SEQ ID NO:7) is suggested. Also, on page 12, under Example 5 in the recitation "osteoclastc". It is believed to be typographical error and it should be corrected to –osteoclastic--. Appropriate correction is required.

## OBJECTION TO IMPROPER MULTIPLE DEPENDENT CLAIMS

5. Claim 6 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only and/or cannot depend from any other dependent claims. See MPEP § 608.01(n). The claim has been treated on the merits and interpreted as dependent solely from the first recited claim from which the claim depends. The claim depends from more than one claim and is not cited in the alternative. Amendment of the claim to recite ".....according to any one of claims 1-5" is suggested.

## STATEMENT OF STATUTORY BASIS, 35 U.S.C. 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 8-10 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153USPQ 678 (Bd. App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). A "use" is not a proper of use claims.

## CLAIMS REJECTION-35 U.S.C. § 112 2nd PARAGRAPH

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite and confusing in the recitation "a therapeutic peptide or a salt thereof" because it is not clear whether the therapeutic peptide is the peptide of SEQ ID NO:7 or other? Further, it is not understood to what "a salt thereof" refer? Is it to a therapeutic peptide or to a pharmaceutical formulation or to both? Appropriate clarification is required.

Claim 3 is indefinite in the recitation "a copolymer of such derivatives" because it is not clear to what kind of copolymer the claim is referring? Also it is not understood what is meant by the term "such derivative"? Appropriate clarification is required.

Claim 6 is indefinite and vague in the recitation "treatment of a human medical condition" because the human medical condition is not defined in the specification nor in the claim, and as such, the metes and bounds of the claim is not met since it encompasses any medical condition.

Claims 8-10 provide for the use of a peptide or a salt in therapy; but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process Applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 10, 11 and 13 are indefinite in the recitation ".....various disorders...." Because it is not clear if Applicant intends a Mrakush format. If Applicant intends to use a Markush format, then, the Office recommends the use of the phrase "……selected from the group consisting of……." In listing species to ensure that the Markush group is "closed".

**CLAIMS REJECTION-35 U.S.C. 112 [1st] PARAGRAPH.**

8. Claims 6-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for employing a pharmaceutical formulation for the release of a peptide or a salt thereof comprising the peptide of SEQ ID NOS:7 and 6

with pharmaceutically acceptable polymer as recited in claims 1-5, does not reasonably provide methods for the treatment of a human medical condition by administering the claimed pharmaceutical formulation (claim 6) or for treatment or protection against disorder of bone growth or disorder of prostate growth (claims 7-9 and 12) wherein the disorder are those recited in claims 10, 11 and 13. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not adequately teach a formulation which is useful in the treatment of human pathologies, including disorders of bone growth (including age-related osteoporosis and osteoporosis associated with post-menopausal hormone status, primary and secondary hyperparathyroidism, disuse osteoporosis, diabetes-related osteoporosis, and glucocorticoid-related osteoporosis) and prostate growth (including benign prostatic hyperplasia and prostate cancer) as recited on page 3, last paragraph in instant specification and as presently claimed in claims 6-13; rather, the specification teaches the preparation, synthesis and microencapsulation of the peptides claimed as disclosed on pages 4-9, Examples 1 and 2, and Tables 1 and 2. Figure I show the effect of increasing doses of GnRH-II on serum calcium concentrations in ovariectomised rats. Examples 3 and 4 teach the analysis of the effects of GnRH-II and analogues on osteogenic cell population *in vitro*. Example 5 shows the expression analysis of GnRH mRNA in osteogenic and osteoclastic II population. Example 6 describes the effect of GnRH-II on bone mineral density in the ovariectomised rat and Example 7 discloses the cellular localization of GnRH-II in paraffin sections of normal

rat bone and human bone. Thus, Examples 3-7demonstrate the biological activity of the peptides of interest as admittedly acknowledged on page 14, paragraph 5, lines 2-3 in the instant specification.

Therefore, the instant specification does not commensurate with the claimed subject matter in which the peptides tested for biological activity against GnRH-ii *in* vitro is expected to be particularly useful in the treatment or protection of all kinds of human pathologies as disclosed above and claimed in claims 6-13. There is no evidence in the instant specification to use or administer the pharmaceutical formulation in therapeutically effective amount as claimed, except for the mere recitation of protocols on pages 2-4 and Examples 3-7 in the instant specification disclosing the preparation of the pharmaceutical formulation without appropriate dosages to be administered for the intended treatment or protection of diseases of the bone and prostates. Further, there are no sufficient data or evidence or working example(s) to substantiate such protocols of using the pharmaceutical formulations of claims 1-5 in the methods of claims 6-13 in the manner claimed. Hence, the only support of the claimed pharmaceutical formulation in the specification is Applicant's supposition of the invention as recited in the protocols. Further, Applicant's claims are directed to a variation of peptides by using specific therapeutically effective amount of pharmaceutical formulation, and there is no objective factual evidence in the specification showing that treatment or prevention has occurred using the specific therapeutically effective amount of pharmaceutical formulation claimed. Hence, one cannot administer specific effective amount of a pharmaceutical formulation in all situation without appropriate testing.

Thus, the claims are based on pure speculation that the method would be effective since Applicant has not established any *nexus* between an effective amount of the claimed peptides and its use in the manner claimed. Therefore, in view of the above, it would include those that have not been shown or taught to be useful or enabled by the disclosed method of making and using the invention. Further, undue experimentation is necessary to determine if and under what conditions, the claimed invention as broadly claimed is enabled, since a vast range of pharmaceutical formulation in a variety of peptides are contemplated and are encompassed as well as wide range of situations (i.e., various kinds of disorders). The results desired appear to be highly dependent on all variables, the relationship of which is not clearly disclosed. Hence, one of ordinary skill in the art would not be able to identify all the pharmaceutical formulations with wide range of dosages intended to effective for the claimed purpose of treatment or prevention of the various disorders as encompassed in the claims would be effective and under what conditions.

Further, the first paragraph of 35 U.S.C. 112 requires, *inter alia*, that a patent specification provide sufficient guidance to enable a person skilled in the art to make and use the claimed invention without undue experimentation. *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991). While patent Applicants are not directed to disclose every species that falls within a generic claim, id. At 496, 20 USPQ2d at 1445, it is well settled that "the scope of the claims must bear a reasonable correlation to the scope of the enablement provided by the specification". *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Where practice of the full scope of

the claims would require experimentation; factors to be considered in determining whether a disclosure would require undue experimentation ..... include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *In re Wands*, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Therefore, in view of the above, and in view of the fact that there is no enablement in the instant specification for methods of treating or preventing a human medical condition or disorders by administering the pharmaceutical formulation in the manner claimed in claims 6-13. Thus, applying the *Wands* factors to the facts of this case, one of skill in the art would find that undue amount of experimentation would be required to practice the full scope of the extremely broad claims fro the reasons given above. Hence, in view of the quantity of experimentation necessary, the lack of adequate guidance or working example(s) or data or evidence, and the breadth of the claims, the claims are not commensurate in scope with the enabling disclosure. Accordingly, filing of evidence commensurate with the scope of the claims or amendment of the claims to what is supported by the enabling disclosure is suggested.

**CLAIM REJECTION-35 U.S.C. § 102(b)**

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 7 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Miyamoto (U.S. Patent No. 4,540,513).

Miyamoto discloses a pharmaceutical formulation comprising a decapeptide having the formula pGlu-His-Trp-Ser-His-Gly-Trp-tyr-Pro-Gly-$NH_2$ which is identical with the claimed SEQ ID NOS:6 and 7 (See e.g. abstract, summary of the invention and claim 1) as directed to claims 1 and 2. With respect to the limitation of the polymer of claim 3, the reference clearly discloses the use of a hydroxy derivative of a carboxylic acid such as acetic acid, and such meets the limitation of claim 3 (See e.g. Examples 1 and 2).

The cited reference above does not disclose the intended use for the controlled release (claims 1 and 2) and for treatment of or for protection against disorders (claims 7 and 11), although, the reference discloses the decapeptide having an excellent gonadotropin releasing activity which meets the limitations of claims 1 and 2; nevertheless, a statement of usefulness or contemplated use of a claimed compound or composition in a claim is usually given little weight in distinguishing over the prior art. *In re Maeder et al.* (CCPA 1964) 337 F2d 875, 143 USPQ 248; *In re Riden et al.* (CCPA 1963) 318 F2d 761, 138 USPQ 112; *In re Sinex* (CCPA 1962) 309 F2d 488, 135 USPQ 302. Further, it is well established that the intended use of a compound (e.g., a polypeptide or a protein or a glycoprotein) does not impart patentability to the compound. *In re Spada,* 911 F.2d 705, 15 USPQ2d 1655 (Fed. Cir. 1990) (The discovery of a new property or use of a previously known composition, even when that property and use are unobvious from the prior art, can not impart patentability to claims

to the known composition); *In re Pearson*, 494 F.2d 1399, 1403, 181 USPQ 641, 644 (CCPA 1974) (intended use of an old composition does not render composition claims patentable); *In re Zierden*, 411 F.2d 1325, 1328, 162 USPQ 102, 104 (CCPA 1969). Thus, in the absence of evidence to the contrary or specific structural limitations, the prior art anticipates the claimed pharmaceutical formulation/product disclosed for controlled release and for treatment or protection against disorder thereof as drafted in claims 1-3, 7 and 11.

10. Claims 1-3, 7 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Folkers et al. (U.S. Patent No. 4,721,775).

The reference of Folkers et al. discloses a pharmaceutical formulation comprising five variations of decapeptides, which is identical with the claimed SEQ ID NO:7 (See e.g. abstract and claims 1-10) as directed to claims 1 and 2. With respect to the limitation of the polymer of claim 3, the reference clearly discloses the use of a hydroxy derivative of a carboxylic acid such as acetic acid, and such meets the limitation of claim 3 (See e.g. col. 4 under Abbreviation and Formulas).

The cited reference above does not disclose the intended use for the controlled release (claims 1 and 2) and for treatment of or for protection against disorders (claims 7 and 11), although, the reference discloses the decapeptide having controlled release activity which meets the limitations of claims 1 and 2; nevertheless, a statement of usefulness or contemplated use of a claimed compound or composition in a claim is usually given little weight in distinguishing over the prior art. *In re Maeder et al.* (CCPA 1964) 337 F2d 875, 143 USPQ 248; *In re Riden et al.* (CCPA 1963) 318 F2d 761, 138 USPQ 112; *In re Sinex* (CCPA 1962) 309 F2d 488, 135 USPQ 302. Further, it is well established that the intended use of a compound (e.g., a polypeptide or a protein or a

glycoprotein) does not impart patentability to the compound. *In re Spada,* 911 F.2d 705, 15 USPQ2d 1655 (Fed. Cir. 1990) (The discovery of a new property or use of a previously known composition, even when that property and use are unobvious from the prior art, can not impart patentability to claims to the known composition); *In re Pearson*, 494 F.2d 1399, 1403, 181 USPQ 641, 644 (CCPA 1974) (intended use of an old composition does not render composition claims patentable); *In re Zierden*, 411 F.2d 1325, 1328, 162 USPQ 102, 104 (CCPA 1969). Thus, in the absence of evidence to the contrary or specific structural limitations, the prior art anticipates the claimed pharmaceutical formulation/product disclosed for controlled release and for treatment or protection against disorder thereof as drafted in claims 1-3, 7 and 11.

11. Claims 1-5, 7 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Tice et al. (U.S. Patent No. 4,835,139).

The reference of Tice et al. discloses a pharmaceutical formulation comprising a decapeptide having the formula pyro Glu-His-Trp-Ser-Tyr-Gly-Leu-Arg-Pro-Gly-$NH_2$ that is identical with the claimed SEQ ID NO:7 (See e.g. col.1, lines 58-62) as directed to claims 1 and 2. The reference also teaches microencapsulation of the peptide by a polymer or a copolymer such as lactide acid and glycolide acid (See e.g. abstract, cols. 3 and Example 1) as directed to claims 3-5.

The cited reference above does not disclose the intended use for the controlled release (claims 1 and 2) and for treatment of or for protection against disorders (claims 7 and 11), although, the reference discloses the decapeptide having controlled release activity which meets the limitations of claims 1 and 2, and for increasing hormone-dependent diseases; nevertheless, a statement of usefulness or contemplated use of a claimed compound or composition in a claim is usually given little weight in

distinguishing over the prior art. *In re Maeder et al.* (CCPA 1964) 337 F2d 875, 143 USPQ 248; *In re Riden et al.* (CCPA 1963) 318 F2d 761, 138 USPQ 112; *In re Sinex* (CCPA 1962) 309 F2d 488, 135 USPQ 302. Further, it is well established that the intended use of a compound (e.g., a polypeptide or a protein or a glycoprotein) does not impart patentability to the compound. *In re Spada,* 911 F.2d 705, 15 USPQ2d 1655 (Fed. Cir. 1990) (The discovery of a new property or use of a previously known composition, even when that property and use are unobvious from the prior art, can not impart patentability to claims to the known composition); *In re Pearson*, 494 F.2d 1399, 1403, 181 USPQ 641, 644 (CCPA 1974) (intended use of an old composition does not render composition claims patentable); *In re Zierden*, 411 F.2d 1325, 1328, 162 USPQ 102, 104 (CCPA 1969). Thus, in the absence of evidence to the contrary or specific structural limitations, the prior art anticipates the claimed pharmaceutical formulation/product disclosed for controlled release and for treatment or protection against disorder thereof as drafted in claims 1-5, 7 and 11.

**CITATION OF RELEVANT PRIOR ART**

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Zohar (U.S. Patent No. 5,288,705) discloses a pharmaceutical formulation for the manipulation of reproduction in fish, which comprises an effective amount of an active compound selected from the group consisting of GnRH, LHRH, GnRH analogs, LHRH analogs and non-toxic salts of any of those compounds embedded in a biocompatible sustained release polymer-based carrier matrix, wherein the biocompatible polymer includes polylactic polyglycolic acids.

WO 97/42987 teaches the use of a pharmaceutical formulation comprising polymer, preferably a poly(lactic-co-glycolic acid) copolymer )PLGA) and an implant comprising a drug such as leutinizing hormone releasing hormone (LHRH) delivered by controlled-release system using microspheres.

## CONCLUSION AND FUTURE CORRESPONDENCE

13. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed number is (571) 272-0955. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The appropriate fax phone number for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 305-7401 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Mohamed/AAM
April 7, 2004

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
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